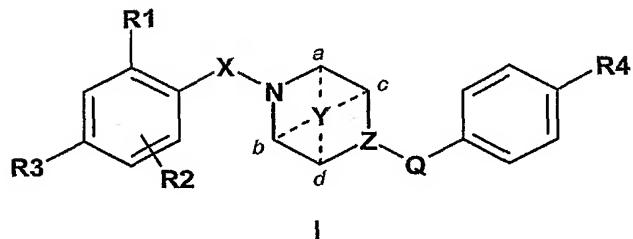


CLAIMS

1. A compound of formula I, or a pharmaceutically acceptable salt or ester thereof,



wherein

R1, R2 and R3 are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, C₁₋₇ alkyl, C₂₋₇ alkyenyl, C₂₋₇ alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicyclic ring for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxaliny or isoquinolinyl;

R4 is selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, C₁₋₇ alkyl, C₂₋₇ alkyenyl, C₂₋₇ alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicyclic ring for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxaliny or isoquinolinyl;

X is -CH=CHCO-;

Y is -(CH₂)_n- where n is 1-6, -CH₂OCH₂- or -CH₂NRCH₂- and is bonded to two of the ring carbon atoms, bonding being to either the ring carbon atoms a and b or the ring carbon atoms c and d; wherein R is selected from the group consisting of H, optionally substituted C₁₋₇ alkyl, carbonyl, acyl, acetyl or sulfonyl;

Z is N or -CH-;

Q is -CH₂- , -NH- or -O-;

wherein when Z is N, Q is CH, and when Z is -CH-, Q is -NH- or -O-;

the optional substituents on R1-R4 are one or more, e.g. 1-3 substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₂₋₇ alkynyl, aryl, heteroaryl, amino, sulfur, sulfinyl, sulfonyl;

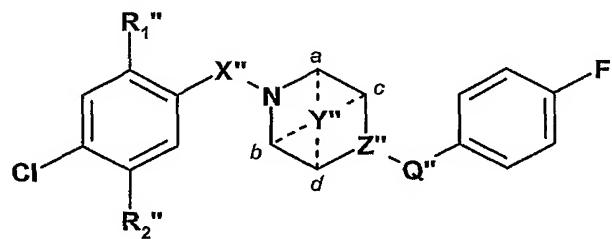
wherein the optionally substituted substituents are optionally substituted once or more by, e.g. 1-6 substituents, a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₂₋₇ alkynyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl.

2. A compound of formula I as defined in claim 1 wherein R1 is an optionally substituted amino, amide, guanidino, sulfonyl, sulfonamide or heterocycloalkyl group, the optional substituents being selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₂₋₇ alkynyl, heterocycloalkyl, amino, sulfur, sulfinyl, sulfonyl;

wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₂₋₇ alkynyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl.

3. A compound of formula I according to claim 1 or 2 wherein R2 is selected from the group consisting of methoxy, trifluoromethoxy, aryl, heteroaryl, C₁₋₇ alkyl.

4. A compound according to any one of the preceding claims, having the formula II, or a pharmaceutically acceptable salt or ester thereof:



wherein

R_1'' and R_2'' are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicyclic for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxaliny or isoquinolinyl;

X'' is $-\text{CH}=\text{CHCO}-$;

Y'' is $-(\text{CH}_2)_n-$ where n is 1-6, $-\text{CH}_2\text{OCH}_2-$ or $-\text{CH}_2\text{NRCH}_2-$ and is bonded to two of the ring carbon atoms, bonding being to either the ring carbon atoms a and b or the ring carbon atoms c and d ; wherein R is selected from the group consisting of H, optionally substituted: C_{1-7} alkyl, carbonyl, acyl, acetyl or sulfonyl;

Z'' is N or $-\text{CH}-$;

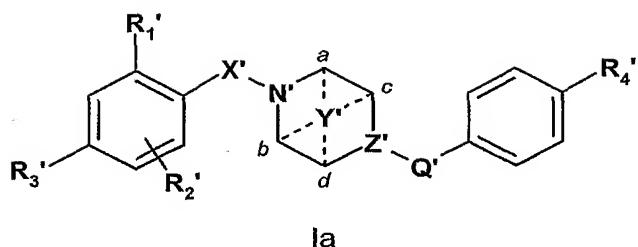
Q'' is $-\text{CH}_2-$, $-\text{NH}-$ or $-\text{O}-$;

wherein when Z'' is N, Q'' is CH, and when Z'' is $-\text{CH}-$, Q'' is $-\text{NH}-$ or $-\text{O}-$;

the optional substituents on R_1'' and R_2'' are one or more, e.g. 1-3 substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, aryl, heteroaryl, amino, sulfur, sulfinyl, sulfonyl;

wherein the optionally substituted substituents are optionally substituted once or more by, e.g. 1-6 substituents, a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl.

5. A compound of formula Ia, or a pharmaceutically acceptable salt or ester thereof,



wherein

R_1' , R_2' and R_3' are independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicyclic for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxaliny or isoquinolinyl;

R_4' is selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, C_{1-7} alkyl, C_{2-7} alkyenyl, C_{2-7} alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicyclic for example butadiene forming napthyl, or heterobutadiene forming quinolinyl, quinoxaliny or isoquinolinyl;

X' is $-OCH_2CO-$ or $-NHCH_2CO-$;

Y' is $-(CH_2)_n-$ where n is 1-6, $-CH_2OCH_2-$ or $-CH_2NRCH_2-$ and is bonded to two of the ring carbon atoms, bonding being to either the ring carbon atoms a and b or the ring carbon atoms c and d ; wherein R is selected from the group consisting of H, optionally substituted: C_{1-7} alkyl, carbonyl, acyl, acetyl or sulfonyl;

Z' is N;

Q' is $-CH_2-$;

the optional substituents on R_1' - R_4' being one or more substituents, independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, C_{1-7} alkyl, C_{2-7} alkenyl, C_{2-7} alkynyl, aryl, heteroaryl, amino, sulfur, sulfinyl, sulfonyl;

wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, C₁₋₇ alkyl, C₂₋₇ alkyenyl, C₂₋₇ alkynyl, amino, sulfur, cycloalkyl, heterocyloalkyl, aryl, heteroaryl.

6. A compound of formula Ia according to claim 5 wherein Y' is -CH₂OCH₂- or -CH₂NRCH₂-.

7. A compound of formula I, Ia, II, Ib or IIb wherein the compound includes a radioisotope selected from the group of ¹¹C, ¹⁸F, ⁷⁵Br, ⁷⁶Br, ⁸⁰Br, ¹²³I, ¹²⁵I, ¹²⁸I, ¹³¹I, ¹³N, ¹⁵O.

8. A compound according to any one of claims 1-7 for use as a pharmaceutical.

9. A compound according to any one of claims 1-7 for use in the treatment of inflammation.

10. A compound according to claim 7 for use as a marker in neuroimaging.

11. A method of inhibiting chemokine receptors or of reducing inflammation in a mammal in need of such treatment which method comprises administering to said subject an effective amount of a compound according to any one of claims 1-7.

12. Use of a compound according to claim 7 as a marker in neuroimaging.

13. A pharmaceutical composition comprising a compound according to any one of claims 1 to 7 in association with a pharmaceutically acceptable diluent or carrier, for use as an immunosuppressant or anti-inflammatory agent.

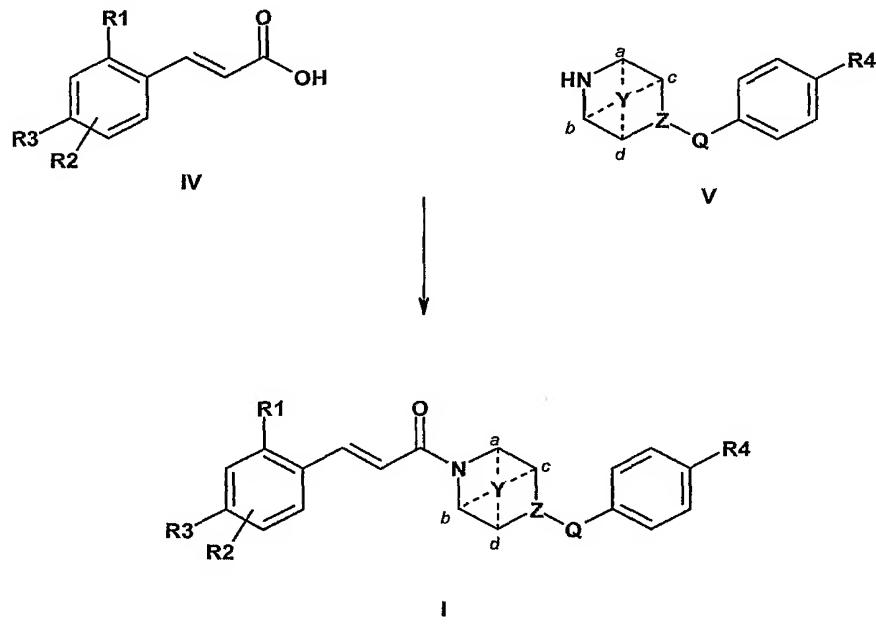
14. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for use as an immunosuppressant or anti-inflammatory agent or for use in the prevention, amelioration or treatment of an autoimmune or inflammatory disease or condition.

15. Use of a compound according to claim 7 in the manufacture of a medicament for the diagnosis of Alzheimer's disease.

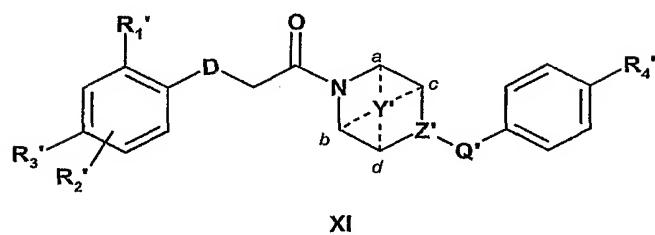
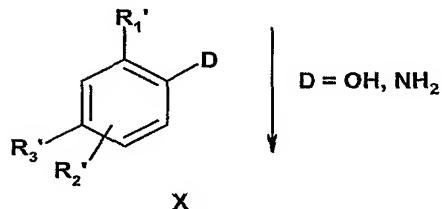
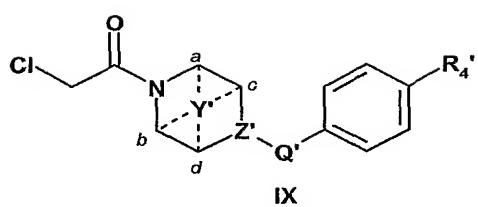
16. A pharmaceutical composition comprising a compound according to claim 7 in association with a pharmaceutically acceptable diluent or carrier, for use as a marker in neuroimaging.

17. A process for the preparation of a compound of formula I, II, Ia, Ib or IIb including the step of:

(a) where the compound is of formula I or II, or of formula Ib or IIb wherein X is -CH=CHCO-, condensing a compound of formula IV with a compound of formula V in the presence of a suitable amide coupling agent, and, where Y is N, deprotection to give the desired compound of formula I (or corresponding compound of formula II, Ib or IIb):

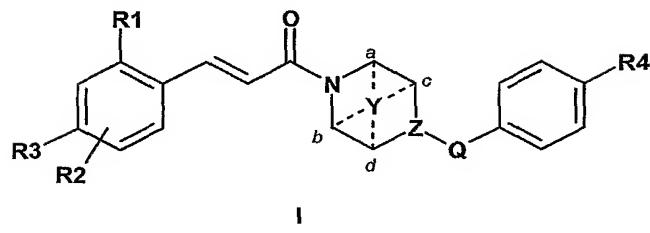
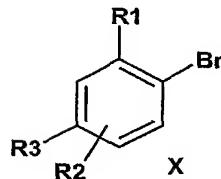
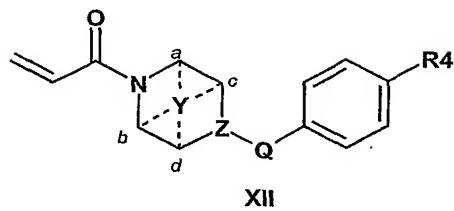


(b) where the compound is of formula Ia or II, or a compound of formula Ib or IIb wherein X is -OCH₂CO-, or -NCH₂CO-, reacting a compound of formula X with a compound of formula IX in the presence of a strong base in an inert organic solvent:



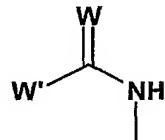
or

(c) where the compound is of formula I or II, or of formula Ib or IIb wherein X is - CH=CHCO-, reacting a compound of formula X with a compound of formula XII in the presence of a suitable reagent such as a palladium catalyst and a base to produce the desired compound of formula I:

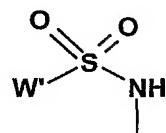


or

(d) where the compound is a compound wherein R1, R_{1'} or R_{1''} is denoted by a group of the following formula:

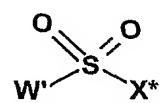
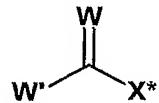


or



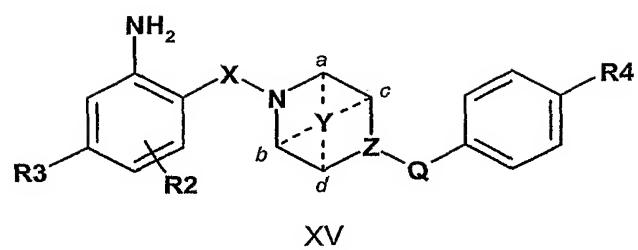
wherein W is O or a nitrogen carrying optional substituents and W' represents optional substituents,

reacting a corresponding compound of formula XII or XIII:



wherein X* represents a leaving group, for example chloro,

with a compound of formula XV:



to produce the desired compound.

18. A process according to claim 17, further including the step of temporarily protecting any interfering reactive groups and/or then isolating the resulting compound of the invention.